Poster III-2

Database Support for Managing and Testing Complex Molecular Cell Biological Hypotheses

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Cell biological hypotheses, often expressed in diagrammatic form as the final slide of a scientific talk or as the last figure in a review article, have become enormously complex. Consequently, dynamic computer models of these systems are beginning to emerge as mainstream tools for data analysis and hypothesis testing in experimental cell biology. In the course of kinetic modeling projects involving the entire secretory pathway (Hirschberg et al. *JCB*, *143 (6) 1485-1503, 1998)*, nuclear protein dynamics (Phair and Misteli, *Nature 404: 604-609, 2000*), the role of Arf1 and COPI in Golgi transport (Presley et al., *Nature 417: 187-193, 2002*) and the dynamics of RNA Pol I transcription (Dundr et al., *Science 298: 1623 - 1626, 2002*) it became clear that a database tool for managing and testing multiple complex hypotheses using data collected in multiple experimental protocols would be useful. Such a tool could allow individual laboratories to advance complex research projects significantly faster.

To this end we have designed and developed a database tool, ProcessDB, built on an Oracle® relational database, that permits cell biologists to enter, manage, modify, and compare multiple working hypotheses for any cell biological system of interest. Particular hypotheses can be chosen for export to modeling and optimization software to make quantitative predictions for a given experimental protocol and for direct comparison of these predictions to experimental data.

ProcessDB is designed from the perspective of molecular cell biology. To use ProcessDB, you enter the molecules, molecular complexes, cellular locations, states (a molecule or a complex in a particular location), and processes (transport, chemical/enzymatically catalyzed reaction, or binding) that constitute each of your working hypotheses. Any collection of entered processes can be assembled as a model in order to support modular construction of large systems. ProcessDB then assists you in translating your qualitative model into a quantitative model expressed as a system of ordinary nonlinear differential equations ready for export to third-party simulation software. A theory's predictions can then be compared directly to your own experimental data or to data from other laboratories.

ProcessDB is thus a new computational tool that aims to support the emerging field of mechanistic knowledge management in molecular cell biological research.

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